CLAIMS

1. A method of screening for a first gene or substance that affects a disease state associated with pain or nociception, or a pain state or nociception, the method comprising:

providing fish with a disease state associated with pain or nociception, or a pain or nociception state, as model fish for screening;

mutating said model fish to provide mutated fish or treating said model fish with a test substance to provide treated fish;

comparing the pain state or nociception of mutated fish or treated fish with the pain state or nociception of model fish in order to identify any mutated fish or treated fish with altered pain state or nociception compared with model fish;

thereby to identify a test substance that affects a disease state associated with pain or nociception, or a pain state or nociception, or, by identifying a genetic difference between model fish and mutated fish with such altered pain state or nociception, to identify a gene that affects a disease state associated with pain or nociception, or a pain state or nociception.

2. A method of screening for a substance or first gene that affects activity or effect of a second gene, or activity or effect of a treatment, on a fish, the method comprising:

providing, as model fish for screening, (i) fish transgenic for the second gene, wherein expression of the second gene provides fish with a disease state associated with pain or nociception, or a pain or nociception state, or

(ii) fish subject to said treatment, wherein the treatment provides fish with a disease state associated with pain or nociception, or a pain or nociception state;

mutating said model fish to provide mutated fish or treating said model fish with a test substance to provide treated fish;

comparing the pain state or nociception of mutated fish or treated fish with the pain state or nociception of model fish in order to identify any mutated fish or treated fish with altered pain state or nociception compared with model fish;

thereby to identify a test substance that affects activity or effect of the second gene or activity or effect of said treatment, or, by identifying a genetic difference between model fish and mutated fish with such altered pain state or nociception, to identify a first gene that affects activity or effect of the second gene or activity or effect of said treatment.

3. The method according to claim 2, comprising mutating model fish transgenic for the second gene to provide mutated fish and identifying a first gene that affects activity or effect of the second gene.

4. The method according to claim 2, comprising treating with a test substance model fish transgenic for the second gene to provide treated fish and identifying a test substance that affects activity or effect of the second gene.

5. The method according to claim 2, comprising mutating model fish subject to said treatment to provide mutated fish

and identifying a first gene that affects activity or effect of said treatment.

6. The method according to claim 2, comprising treating with a test substance model fish subject to said treatment to provide treated fish and identifying a test substance that affects activity or effect of said treatment.

7. The method according to any one of claims 1, 2, 4 or 6, wherein the test substance lessens activity or effect of the second gene or said treatment.

8. The method according to any one of claims 1, 2, 4 or 6, wherein the test substance enhances activity or effect of the second gene or said treatment.

9. The method according to any one of claims 1, 2, 3 or 5, wherein the first gene lessens activity or effect of the second gene.

10. The method according to any one of claims 1, 2, 3 or 5, wherein the first gene enhances activity or effect of the second gene.

11. The method according to any one of the preceding claims, wherein the first gene or test substance has an analgesic effect.

12. The method according to any one of claims 2 to 11, wherein the second gene is involved in pain transduction.

13. The method according to any one of the preceding claims, further comprising screening for a further test

substance that interacts with the protein encoded by the first gene or the test substance.

14. The method according to claim 13, further comprising identifying and/or obtaining the further test substance.

15. The method according to claim 13 or claim 14, wherein the interaction has a synergistic or additive effect.

16. The method according to claim 13 or claim 14, wherein the interaction between the test substance and the protein encoded by the first gene has a deleterious effect.

17. The method according to any one of the preceding claims, wherein the pain state or nociception is assessed by the measurement of a behaviour.

18. The method according to claim 17, wherein the behaviour is the relative position of fish in a gradient induced by one or more stimuli.

19. The method according to claim 18, wherein when more than one stimulus is used, the stimuli are applied sequentially.

20. The method according to claim 18 or claim 19, wherein a stimulus is gradable such that it can be quantitated.

21. The method according to claim 20, wherein a stimulus is gradable by the use of opposing stimuli.

22. The method of any one of claims 18 to 21, wherein one or more stimuli are selected from the group consisting of

light stimuli, optomotor stimuli, temperature, food, aversive chemicals or drugs, attractive or additive chemicals or drugs, physical aversion stimuli such as electric shock or threatening shape, mechanical stimuli and depth of water.

23. The method according to any one of claims 17 to 22, wherein the pain state or nociception is further assessed by the measurement of the expression of one or more genes.

24. The method according to any one of claims 17 to 22, wherein the pain state or nociception is further assessed by the measurement of calcium fluxes.

25. The method according to any one of the preceding claims, wherein the fish is selected from the group consisting of zebrafish, fugu, goldfish medaka and giant rerio.

26. The method according to claim 24, wherein the fish is a zebrafish.

27. A fish model for a disease state associated with pain or nociception, or a pain state or nociception, for screening for a substance or first gene that affects activity or effect of a second gene, or activity or effect of a treatment, on a fish, comprising (i) a fish transgenic for the second gene, wherein expression of the second gene induces a disease state associated with pain or nociception, or a pain or nociception state, or (ii) a fish subject to the treatment, wherein the treatment induces a disease state associated with pain or nociception, or a pain or nociception state.

28. The fish model according to claim 27, wherein the second gene is involved in pain transduction.

29. The fish model according to claim 27 or claim 28, wherein the pain state or nociception of the fish is assessed by the measurement of behaviour.

30. The fish model according to claim 29, wherein the behaviour is the relative position of fish in a gradient induced by one or more stimuli.

31. The fish model according to any one of claims 27 to 30, wherein the fish is selected from the group consisting of zebrafish, fugu, goldfish medaka and giant rerio.

32. The fish model according to claim 31, wherein the fish is a zebrafish.